IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

| | | |
|---|---|---|
| VIIV HEALTHCARE UK LTD. and VIIV HEALTHCARE CO., | ) | |
| Plaintiffs, | ) | |
| v. | ) | Civil Action No. 11-CV-00576-RGA (Consolidated) |
| LUPIN LTD. and LUPIN PHARMACEUTICALS, INC., et al. | ) | |
| Defendants. | ) | |

**LUPIN'S RESPONSIVE POST-TRIAL BRIEF REGARDING NO INFRINGEMENT**

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## CASES

**STATUTES**



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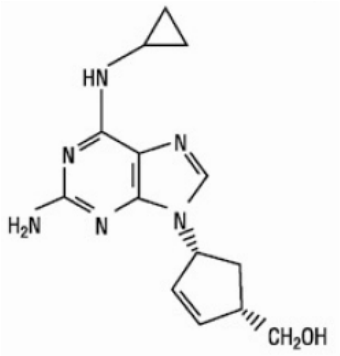
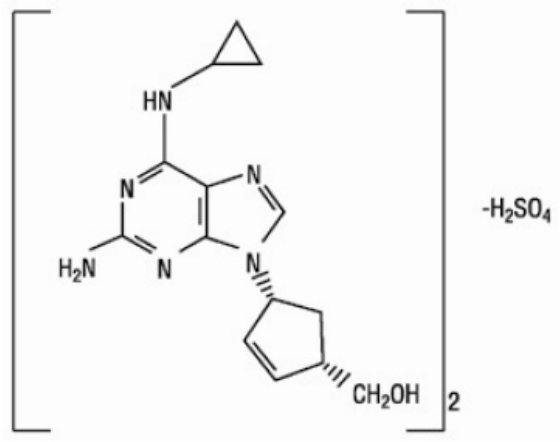
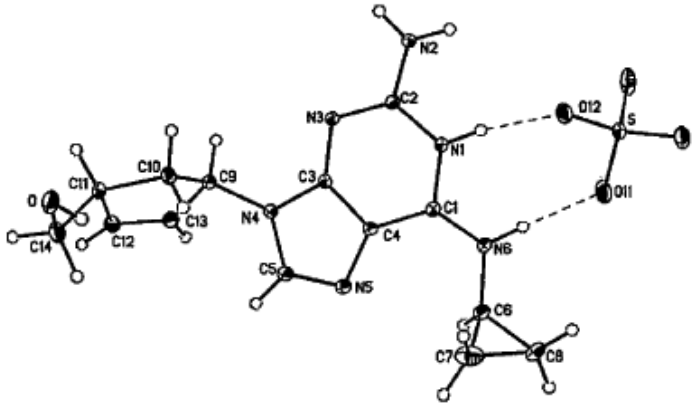
## List of Abbreviations

| Abbreviation | Reference | Trial Exhibit or D.I. Number (if applicable) |
|---|---|---|
| '191 patent | U.S. Patent No. 6,417,191 | JX 1 |
| Abacavir free base, or 1592U89 | (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, which has the following chemical structure:  | - |
| "1S-methanol" element | Abbreviation for the claim language, "(1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol." | - |
| Abacavir sulfate | (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol sulfate salt (2:1), which can be depicted as follows:  or | PTX 152 at 012355 |

| | | |
|---|---|---|
| |  | LTX 1288 at 866 |
| ANDA | Abbreviated New Drug Application | - |
| Lamivudine or 3TC | (2R, cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one | - |
| AZT | Zidovudine | - |
| FDA | Food and Drug Administration | - |
| RT enzyme | Reverse transcriptase enzyme | - |
| Tr. 1-386 | Official Transcript of Bench Trial (Day 1) held on 06-24-13 before Judge Richard G. Andrews | D.I. 192 |
| Tr. 399-784 | Official Transcript of Bench Trial (Day 2) held on 06-25-13 before Judge Richard G. Andrews | D.I. 193 |
| Tr. 785-1154 | Official Transcript of Bench Trial (Day 3) held on 06-26-13 before Judge Richard G. Andrews | D.I. 194 |
| Tr. 1155-1487 | Official Transcript of Bench Trial (Day 4) held on 06-27-13 before Judge Richard G. Andrews | D.I. 195 |
| Tr. 1488-1600 | Official Transcript of Bench Trial (Day 5) held on 06-28-13 before Judge Richard G. Andrews | D.I. 196 |

## I. PRELIMINARY STATEMENT.

ViiV's infringement analysis presumes its claims cover any "abacavir" derivative or product that transiently produces abacavir free base *in vivo*. ViiV's claims do not cover the Lupin ANDA product's abacavir sulfate salt or any *in vivo* conversion product. ViiV also presented no "symptoms or effects" evidence besides its experts' opinions that the phrase does not exclude treating an HIV infection—effectively eviscerating the "symptoms or effects" claim element. (*See, e.g.*, Tr. at 82:14-19). ViiV presented no evidence Lupin intends for its ANDA labeling to induce doctors to treat *symptoms or effects* of HIV, such as pneumonia, cytopenic purpura, or Kaposi's sarcoma, etc. ViiV thus failed to prove Lupin's ANDA Product infringes any Asserted Claim of the '191 patent (4, 26, 27, 29, 30, 34, 36, 38, 39, and 47).

ViiV also failed to justify its remedy request—a permanent injunction—against Lupin Ltd. or Lupin Pharmaceuticals Inc. (D.I. 1 at 6). Judgment should be entered in Lupin's favor.

## II. VIIV HAS NOT MET ITS BURDEN ON INFRINGEMENT OR REMEDIES.

### A. Legal standards.

In an ANDA case, whether the manufacture, use, or sale of the drug would infringe the patent "is properly grounded in the ANDA application and the extensive materials typically submitted in its support." *Bayer AG v. Elan Pharm. Res. Corp.*, 212 F.3d 1241, 1248 (Fed. Cir. 2000) (citation omitted). Infringement is a two-step analysis where "[f]irst, the claims are construed" and next "compared to the accused device." *Id.* at 1247. ViiV must show that "every limitation of the patent claim asserted" is satisfied "either literally or by an equivalent." *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988).

Any missing limitation means "there is no literal infringement as a matter of law." *Bayer*, 212 F.3d at 1247. For the doctrine of equivalents, an equivalent of a missing element is found only if "insubstantial differences" distinguish the missing claim element from the accused

product. *Abbott Labs. v. Novopharm Ltd.*, 323 F.3d 1324, 1329 (Fed. Cir. 2003).

ViiV cannot meet its burden by comparing Lupin's ANDA product to its own; asserting Trizivir is a commercial embodiment[1]; or by asserting bioequivalence. *See Zenith Labs., Inc. v. Bristol-Myers Squibb Co.*, 19 F.3d 1418, 1423 (Fed. Cir. 1994) ("it is error" to compare to the patentee's alleged commercial embodiment; "the only proper comparison is with the claims of the patent"); *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1298 (Fed. Cir. 2009) (therapeutic equivalence for FDA purposes is a regulatory/medical concern; "equivalency for purposes of patent infringement requires an element-by-element comparison of the patent claim and the accused product, requiring not only equivalent function but also equivalent way and result").

**B. Lupin does not infringe because it uses abacavir sulfate, not free base.**

ViiV's case ultimately hinges on a new and incorrect claim construction theory: that a chemical name claim element covers not just abacavir free base, but simultaneously its salts.

**1. Claim construction—the "1S…methanol" chemical language defines the free base structure alone, not its salts or other derivatives.**

ViiV asserts "Lupin contends that the asserted patent claims are directed to 'abacavir free base' ***(though the term appears nowhere in the patent)***…." (D.I. 203, Pl. Br. at 8) (emphasis added). All Asserted Claims include this chemical name element: "(1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol" (the "1S-methanol" element). Dr. Langer, ViiV's expert, admitted this chemical name ***defines the abacavir free base*** structure:

Q: We agree that the chemical name for abacavir is (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol; right?
A. Yes, very good.
Q. All right. ***And that chemical nomenclature defines the structure we would call the abacavir freebase***; is that true?
A. ***That's fair. Right***.

[1] ViiV incorrectly states "Trizivir® contains the 'triple combination' of abacavir, 3TC, and AZT." (D.I. 203, Pl. Br. at 3). Trizivir contains abacavir ***sulfate*** as the active ingredient. (Tr. 229:12-15). Trizivir does not meet the Asserted Claims either.

(Tr. 209:13-22) (emphasis added). The "1S-methanol" chemical language element thus defines abacavir as the free base structure alone. (Tr. 251:4-252:6, 257:11-20).

Despite its expert's admission, ViiV cites *Merck & Co. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367 (Fed. Cir. 2003) to argue the "1S-methanol" chemical language should *also* be construed as covering a salt. (D.I. 203, Pl. Br. at 9-10); *Merck & Co. v. Teva Pharms. USA, Inc.*, 228 F. Supp. 2d 480, 486 (D. Del. 2002) (noting acid/salt question was a claim construction issue, where "the specification defines the term by implication"). In *Merck*, the district court described the specification's separate "chemistry" and "biology" sections. *Id*. at 489. The Federal Circuit explained that the biology section used the claimed chemical name to describe both an acid and salt. *Merck*, 347 F.3d at 1370 ("throughout the specification the inventors described the acid active agent as encompassing the acid and its salt forms"). With only a method claim issued, the district court applied only the "biology" section's chemical name usage, while specifically noting the construction might have been different if claim 1 "were still a composition claim" since then the chemistry section "would be highly instructive." *Merck*, 228 F. Supp. 2d at 489. The Federal Circuit noted the published literature used the particular "acid" chemical nomenclature *even when describing a compound that was clearly the sodium salt*. *Merck*, 347 F.3d at 1370 ("the structure of the sodium salt is labeled both as 'Alendronate' and as '4-amino-1-hydroxybutylidene 1,1 bisphosphonic acid'"). Thus, the Federal Circuit agreed this *particular* name had a lexicography definition that included salts. *Merck*, 347 F.3d at 1371.

The patentee failed to demonstrate a similar lexicography definition in the same bisphosphonate field as *Merck* in *Hoffmann-La Roche Inc. v. Apotex Inc.*, Nos. 07-4417 *et seq.*, 2010 WL 1875569 (D.N.J. May 10, 2010) ("*Roche*"). In *Roche*, the patent claims included a chemical name, "1–hydroxy–3–(N–methyl–N–pentylamino)–propane–1,1–diphosphonic acid."

2010 WL 1875569, at *3. Roche insisted this name included the salt; the generics argued the chemical name was limited to the "free acid form only." *Id.* The district court found no *Merck*-like lexicography since Roche's specification "clearly differentiate[d] between free acids and salts," and the claims followed the acid chemical name "*with the phrase 'and the physiologically active salt.'*" *Id.* at *4 (emphasis added). If the acid name presumptively covered salts, it would have been "both redundant and unnecessary to claim both [the chemical name] 'and the physiologically active salt form thereof.'" *Id.* at *3 n.3.

The '191 patent's specification and claims are analogous to *Roche*, not *Merck*. Unlike *Merck*, there is no separate "chemistry" and "biology" section where the latter uses salts under the "1S-methanol" chemical name. Like *Roche*, the '191 patent's specification gives a drug name, followed by a separate salt description or the term "or physiologically functional derivatives of any thereof."[2] (*See, e.g.*, JX 1 at col. 1, ll. 9-11 (chemical name followed by "1592U89"); col. 5, ll. 38-43 ("a unitary dosage form comprising at least…, 1592U89…or physiologically functional derivatives of any thereof"); col. 2, ll. 18-20 ("the present invention provides a combination comprising 1592U89 or a physiologically functional derivative thereof"); col. 3, ll. 18-21 ("For therapeutic use, salts of 1592U89…will be physiologically acceptable, i.e. they will be salts derived from a physiologically acceptable acid or base")). This distinction between free base and salt also appears in the '191 patent claims, *e.g.*, claim 16:

> **16**. A pharmaceutical formulation comprising (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof in association with one or more pharmaceutically acceptable carriers therefor.

[2] "Physiologically functional derivative" was construed to include any "physiologically acceptable salt… of 1592U89 [abacavir]…" (D.I. 126 at 3; JX1 at col. 2, ll. 32-39).

(JX 1 at col. 13, ll. 45-53). Dr. Langer also testified that "abacavir sulfate is a physiologically functional derivative of abacavir." (Tr. 209:23-210:11; *see also* Tr. 207:22-208:4 (opining "physiological functional derivatives" includes "salts and solvates")).

ViiV emphasizes specification statements that "therapeutic use" of the active ingredients included "salts of 1592U89," which, "whether or not derived from a physically acceptable acid or base, are within the scope of the present invention." (D.I. 203, Pl. Br. at 10 (citing JX 1 at col. 3, ll. 25-27). First, this language nowhere suggests the "1S-methanol" claim element presumptively means salts. Dr. Langer admitted 1592U89 refers to abacavir as the free base. (Tr. 211:1-4). Stating "***salts of*** 1592U89," and that salts can be ***derived from*** an acid or base confirms salts *differ from* the originating acid or base. Second, Lupin does not argue the specification *never* contemplated salts—it plainly does, as evidenced by, *e.g.*, the discussion at col. 3, lines 3-28. But the mere fact that an embodiment is discussed and covered by unasserted claims does not warrant adopting a non-ordinary meaning for the "1S-methanol" claim element so the presently-Asserted Claims presumptively include all salts. *Cf. Lucent Techs., Inc. v. Gateway, Inc.*, 525 F.3d 1200, 1214-16 (Fed. Cir. 2008) (explaining if a claim is unambiguous, "we have construed the claims to exclude all disclosed embodiments").

ViiV suggests the "1S-methanol" claim element includes salts because claim 32 uses the free base chemical name, and dependent claim 35 references the succinate salt. (D.I. 203, Pl. Br. at 10-11). But ViiV ignores that claim 48 also uses the "1S-methanol" element followed by "**or** a physiologically functional derivative thereof," with dependent claim 49 stating the "***physiologically functional derivative of*** (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol is the succinate salt." (JX 1 at col. 16, ll. 5-16). Given how ViiV rotely regurgitated dependent claim elements (*e.g.*, claims 35 and 40 are also improper

dependent claims because they are identical to one another and refer to the identical underlying claim), the conclusion to draw from claim 35 is not that ViiV signaled a redefinition of the "1S-methanol" element via lexicography, but that its regurgitation yielded improper dependent claims as in *Pfizer, Inc. v. Ranbaxy Lab. Ltd.*, 457 F.3d 1284, 1291-92 (Fed. Cir. 2006).[3]

Thus, since the now-Asserted Claims only use the "1S-methanol" claim language, they are limited to abacavir free base, and do not cover salts. (Tr. 251:4-252:9, 261:3-262:18).

**2. Comparison of the accused product to what is claimed—the Lupin ANDA product uses abacavir sulfate, not free base.**

With the "1S-methanol" element construed as limited to its ordinary meaning—abacavir free base—ViiV cannot meet its burden of proof for the Lupin ANDA product.

**a. Lupin's ANDA product contains only the abacavir sulfate salt.**

ViiV admits Lupin's ANDA must conform to 21 U.S.C. § 355(j)(2). (D.I. 203, Pl. Br. at 3-4). But Subsection (j)(2)(A)(ii) requires an ANDA to include the same "active ingredient" as the reference listed drug, a standard not met by a free base vs. salt.[4] Every ANDA section ViiV introduced into evidence expressly recognizes and defines the active ingredient in Lupin's ANDA product as "abacavir sulfate," a sulfate salt, not abacavir free base. (*See* PTX 135 at 000001 ("Established name…Abacavir Sulfate"); PTX 136 at 000015 ("Lupin Limited herewith submits an … (ANDA) for Abacavir Sulfate…"); PTX 137 at 000044, 48 (referencing drug master file for "Abacavir Sulfate"); PTX 140 (product defined as "Abacavir Sulfate … Tablets"); PTX 142 at 000279 (general drug name is "Abacavir Sulfate", chemical name is "(1S, 4R)- 4-[2-

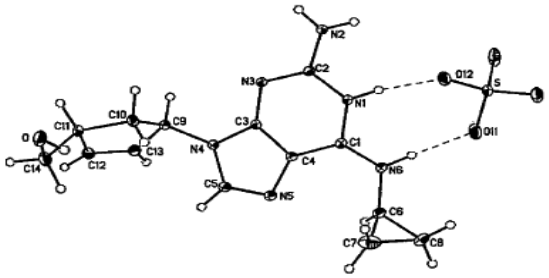
[3] ViiV tries to distinguish *Pfizer*, but Pfizer, like ViiV, tried to apply *Merck* to have acid claims cover salts, and failed since "the intrinsic evidence would not have supported such an interpretation…." *Pfizer*, 457 F.3d at 1291 n.6. *Pfizer* confirms ViiV cannot use an improperly dependent claim to expand the ordinary meaning of the "1S-methanol" claim language; a genuine lexicography definition in the specification is required.

[4] *See* 54 Fed. Reg. 28872, 28878 (July 10, 1989) (FDA considers a salt of an active ingredient to be "a different active ingredient, and will not approve petitions that seek permission to submit an ANDA for a drug product which substitutes a different salt or ester of an active ingredient….").

Amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-***methanol sulfate (2:1)***") (emphasis added); PTX 145 at 000339 (core composition is "Abacavir Sulfate Layer" of 351.380 mg, equivalent to 300 mg abacavir); PTX 150 at 001609 (same, with equations for converting sulfate salt amounts); PTX 154 (repeatedly listing abacavir sulfate as the active ingredient)). The Lupin proposed ANDA labeling expressly defines the active ingredient as the sulfate salt (2:1):

> **Abacavir Sulfate**
>
> The chemical name of abacavir sulfate is (1*S*,*cis*)-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol sulfate (salt) (2:1). Abacavir sulfate is the enantiomer with *1S*,

(PTX 152 at 012355). ViiV's expert admitted the salt structure differs from abacavir free base (Tr. 215:8-217:6), and that to get from abacavir free base to the sulfate salt requires a chemical reaction that changes, among other things, the molecular weight. (Tr. 217:7-23). The resulting salt has fundamentally different properties. (Tr. 254:23-255:13, 257:17-23). This goes beyond a mere mixture; Dr. Langer acknowledged that if a person held just the $H_2SO_4$ "sulfate" part in his hand, he would experience chemical burns. (Tr. 212:4-18). The literature illustrates the abacavir salt structure's new bonds and describes their effect. The salt, not free base, forms an infinite structural chain as a result of the new shared chemical bonds (dotted lines below):




(LTX1288 at 865-66; Tr. 225:3-226:22). To derive "abacavir" free base from the sulfate salt requires fundamentally destroying the salt structure itself. (Tr. 262:11-18, 256:15-257:4).

**b. ViiV's selective "abacavir" focus should be disregarded.**

ViiV musters up artificially cropped quotes to support its position in its brief at pages 7-8; read in context, none constitute an admission that Lupin's ANDA tablets contain abacavir free

base.[5] The deposition testimony cited likewise never asked the witnesses to identify *the active ingredient* in the Lupin tablets; in testimony ViiV does not cite, Mr. Dahibate confirmed that the active ingredient in the tablet is abacavir sulfate. (Tr. at 152:13-153:19). Likewise, that abacavir may transiently result *after* the tablet is administered, swallowed by a patient and the tablet and salt are chemically destroyed (Tr. 256:15-257:4, 262:15-18, 290:23-294:3), is irrelevant to what is in the product that Lupin actually prepares under its ANDA.

ViiV theorizes abacavir salts satisfy the "1S-methanol" element because abacavir is "in" the salt. (D.I. 203, Pl. Br. at 8). ViiV offered ***no*** evidence the free base structure remains intact and unreacted in the salt. Dr. Langer admitted the sulfate salt has new chemical bonds missing from the free base structure. (Tr. 228:1-13). The sulfate salt's crystal structure and Dr. Arnold's testimony both confirm the salt has a different molecular weight and chemical bond arrangements. (LTX1288; Tr. 263:22-264:3, 294:15-295:3). ViiV's alternative theory fails.

ViiV also suggests it is relevant that abacavir salts can be destroyed *in vivo* to "provide" abacavir free base. (D.I. 203, Pl. Br. at 9). First, none of ViiV's evidence for the other claim elements involving doses, ratios, combined formulation, tablets, etc., involves the *in vivo* temporal state, after a patient has swallowed a tablet and the tablet has been fundamentally destroyed. Dr. Langer's testimony for such elements was limited to a pre-ingested tablet. (Tr. 187:13-22, 188:9-189:4, 191:7-192:12, 199:7-16, 199:19-200:6, 200:13-201:2). Second, by the time the tablet and sulfate salt is destroyed, the other drugs are also freed as well—and ViiV has no evidence these other drugs remain as part of a combination. (*See*, *e.g.*, PTX140 at 001720).

[5] ViiV's citation to PTX 135 *excludes* the preceding language that reads, "abacavir sulfate … is one of multiple products containing abacavir". (PTX135 at LUPIN(TRIZ) 000003). ViiV's first citation to PTX 152 at 012337 excludes the end citation (3), referring to Section 3 of the label, which at 012341 more completely explains the dosage form contains "300 mg of abacavir ***as abacavir sulfate.***" ViiV's second and third PTX 152 citations fare no better, again eliminating the preceding "abacavir sulfate" language. PTX 154 repeats this same language from PTX 152.

Third, no claim calls for a formulation to "release," "provide" or "produce" abacavir. Fourth, the actual ingredient that performs the therapeutic work *in vivo* is the metabolite carbovir triphosphate, which also has a different structure compared to the free base and could only fall within unasserted "physiologically functional derivative" claims. (Tr. 213:24-214:7, 291:4-12).

Thus, there is no avenue by which ViiV can meet its infringement burden for *all* elements of the asserted claims at one point in time. Lupin also addresses each claim individually below.

**c. Claim 47 is not literally or equivalently infringed.**

A dependent claim cannot be infringed without first demonstrating infringement of the underlying independent claim. *Wahpeton Canvas Co. v. Frontier, Inc.*, 870 F.2d 1546, 1553 (Fed. Cir. 1989). Claim 47 depends on claims 45 and 46. Claim 45 reads as follows:

> 45. A pharmaceutical formulation comprising (1S, 4R)-cis-4-[2-amino-6-(cyclopropyl-amino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, and [3TC] in a ratio of 1 to 20:1 to 20:1 to 10 by weight, in association with one or more pharmaceutically acceptable carriers therefor.

(JX 1 at col. 15, ll. 15-21). Claim 47 requires this formulation to be, *e.g.*, a tablet. (*Id*. ll. 3-4).

***No Literal infringement***. Claim 45's "1S-methanol" element limits the claimed formulation to one with abacavir as the free base; Lupin's ANDA product uses abacavir sulfate salts beyond the claimed scope. ViiV's *in vivo* conversion theory is inapplicable because by the time the abacavir salt is destroyed *in vivo*, the tablet is also destroyed. (Tr. 262:6-18, 290:13-22).

***No infringement by equivalents***. ViiV paraphrases Dr. Langer's testimony that since both abacavir and abacavir sulfate are both "used to treat the symptoms of HIV" *in vivo* by "inhibiting a particular enzyme" to suppress HIV replication, they must be equivalent. This fails as a matter of fact; the compound inhibiting HIV replication is carbovir triphosphate—not the free base. (Tr. 213:24-214:7, 291:4-12).[6] A salt's function in a tablet is to impart greater

[6] Again, if ViiV wants to focus on *in vivo* circumstances for the "1S-methanol" element, it must likewise show how all other elements apply *in vivo*—but ViiV lacks evidence that these other

stability and handling properties. (Tr. 220:19-24, 254:20-255:13). ViiV offered no testimony that these qualities are equally met by abacavir free base and abacavir sulfate.

ViiV's equivalents theory also fails as a matter of law. *First*, ViiV mischaracterizes the prohibition against vitiating a claim element. The Federal Circuit has never held that only an "antithesis" constitutes vitiation, and does not so hold in the cases ViiV cites. *E.g.*, *Pfizer, Inc. v. Teva Pharms. USA, Inc.*, 429 F.3d 1364, 1379-80 (Fed. Cir. 2005) ("There is no set formula for determining whether a finding of equivalence would vitiate a claim limitation … courts must consider the totality of the circumstances of each case….").[7] Here, the claims include a specific chemical name that defines a single structure; the salt materially alters that structure producing a compound with different molecular weights and properties. (Tr. 255:14-256:4, 257:17-23, 263:22-264:3). ViiV cites no evidence such *structural* differences are insubstantial.

*Second*, ViiV suggests the public dedication doctrine does not apply, citing *Pfizer*, 429 F.3d at 1379. All *Pfizer* recognizes is that for there to be a disclosure by dedication, reference to a genus does not presumptively dedicate all species within it to the public; the "disclosure must be of such specificity that one of ordinary skill in the art could identify the subject matter that had been disclosed and not claimed." *Id*. at 1378. Since the doctrine of equivalents protects patentees who could not claim *unforeseen* equivalents, subject matter specifically disclosed but unclaimed, is not a viable equivalent as a matter of law. *Abbott*, 566 F.3d at 1297.

Lupin did not need to ask Dr. Arnold to opine on this issue (D.I. 203, Pl. Br. at 11),

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elements are literally or equivalently met once the tablet is destroyed. Indeed, a destroyed tablet is surely the antithesis of the required tablet claim element.

[7] When a proposed equivalent is the antithesis of what is claimed, *no reasonable jury* could deem it an equivalent, rendering judgment as a matter of law appropriate. *See Moore U.S.A., Inc. v. Standard Register Co.*, 229 F.3d 1091, 1106 (Fed. Cir. 2000) ("[I]t would defy logic to conclude that a minority—the very antithesis of a majority—could be insubstantially different from a claim limitation requiring a majority, and no reasonable juror could find otherwise.").

because Dr. Langer admitted the '191 patent specification disclosed sulfate salts at col. 3, line 14. (Tr. 211:16-212:9). Dr. Langer opined the sulfate salt meets the "physiologically functional derivative" language in non-asserted claims. Since ViiV "clearly knew of the [sulfate] forms of the claimed invention because it claimed and disclosed them" elsewhere in the '191 patent, but "declined to claim" this expressly disclosed embodiment in the Asserted Claims, that "foreclos[es] any recapture under the doctrine of equivalents." *Abbott*, 566 F.3d at 1297 (citing *Johnson & Johnston Assocs. v. R.E. Serv. Co.*, 285 F.3d 1046, 1054 (Fed. Cir. 2002)).

**d. Method claims 4, 26, 27, 29, 30, 34, 36, 38 and 39.**

ViiV asserts Lupin's abacavir sulfate tablets infringe claims 4, 26, 27, 29, 30, 34, 36, 38 and 39 not directly (D.I. 203, Pl. Br. at 13), but indirectly, because "those claims recite the delivery of therapeutically effective amounts of the active ingredients" (*id*. at 18) to "provide abacavir" *in vivo*. The claims do not cover what is ***delivered or provided*** to patients *in vivo*.

Claim 4 discusses treating an animal "with a therapeutically effective amount of a combination" (via claim 1) where the combination has active ingredients "present in a ratio" of a certain type as measured "by weight". Likewise, the remaining claims discuss treating an animal with a drug <u>combination</u> where the active ingredients are "present in an amount from 5 to 1000 mg per unit dosage form," "administered simultaneously," or are present in a "single combined formulation." These combinations, ratios, weight percentages and dose amounts evaluate what is *in a pharmaceutical formulation*, and indeed Dr. Langer's infringement analysis was limited to what is in the Lupin tablet. (Tr. 187:13-22, 188:9-189:4, 191:7-192:12, 199:7-16, 199:19-200:6, 200:13-201:2). ViiV <u>never</u> presented evidence at trial or in its brief that these amounts, ratios, combinations etc. survive together *in vivo* during the brief point in time when abacavir sulfate has been destroyed and released from a dissolved tablet, but prior to being metabolized to carbovir triphosphate. (Tr. 199:7-16, 200:11-201:2, 289:17-291:12; D.I. 203, Pl. Br. at 12-13).

Thus, neither Lupin nor patients using the product directly or indirectly infringe the method claims, because the methods focus on what is administered to the patient or animal in the treatment method, not what occurs in the body. *See, e.g., Schering Corp. v. Glenmark Pharms. Inc., USA*, No. 07-1334, 2008 WL 4307189, at *8 (D.N.J. Sept. 16, 2008) ("the term 'administering'…includes *only* administering the pharmaceutical compound…and not the metabolite that forms *in vivo* upon administration"). Further, what actually works *in vivo* to inhibit the RT enzyme is carbovir triphosphate, not the free base. (Tr. 291:4-12). With no direct infringement via the tablet, there is no inducement even if *in vivo* activity is considered. *Novartis Pharms. Corp. v. Eon Labs. Mfg., Inc.*, 363 F.3d 1306, 1308 (Fed. Cir. 2004).

**e. Claim 4 does not include physiologically functional derivatives.**

ViiV asserts without analysis that the physiologically functional derivative language survived through to method claim 4. (D.I. 203, Pl. Br. at 18). Lupin explained why this was not so at closing argument. (Tr. 1558:1-1560:3). This also can be illustrated by comparing claim 4 and claim 13, which both depend from independent claim 1, side by side:

**4**. A method according to claim **2** wherein (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, and (2R, cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one are present in a ratio of 1 to 3:1 to 3:1 to 2 by weight.

**13**. A method according to claim **1** wherein (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-3-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically function derivative thereof, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof are present in a ratio of 1 to 10:1 to 10:1 to 5 by weight.

Claim 4 eliminated the "or a physiologically functional derivative" thereof language from claim 1; claim 13 preserved it; while both dependent claims add the additional weight ratio limitations. This confirms that when the patentees wanted to carry forward the "physiologically functional derivative" language into subsequent dependent claims, they did so and knew how to do so. That claim 4 excludes the phrase means the "physiologically functional derivative" option is beyond claim 4's scope. *Sage Prods., Inc. v. Devon Indus., Inc.*, 126 F.3d 1420, 1425 (Fed. Cir. 1997)

("as between the patentee who had a clear opportunity to negotiate broader claims but did not do so, and the public at large, it is the patentee who must bear the cost of its failure to seek protection…."); *see also CAE Screenplates Inc. v. Heinrich Fiedler GmbH*, 224 F.3d 1308, 1317 (Fed. Cir. 2000) ("In the absence of any evidence to the contrary, we must presume that the use of these different terms in the claims connotes different meanings."). Thus, claim 4 lacks any "physiologically functional derivative" element to apply to Lupin's ANDA product.

***Summary***. In view of the above, ViiV has not met its burden of proof of direct infringement by anyone for the Asserted Claims on either literal or equivalent infringement.

### C. There is no indirect infringement by Lupin based on its labeling, particularly as to the "symptoms or effects" language.

For method of treatment claims, the only "hook" for generic infringement arises based on statements made in the proposed ANDA labeling. *See, e.g., Warner-Lambert Co. v. Apotex, Corp.*, 316 F.3d 1348, 1364 (Fed. Cir. 2003) ("[T]he ANDA must be judged on its face for what an accused infringer seeks the FDA's approval to do."); *AstraZeneca Pharms. LP v. Apotex Corp.*, No. 10-584, 2010 WL 5376310, at *14 (D. Del. Dec. 22, 2010) (for method claims, "a court need only compare the ANDA's proposed labeling…to the indications claimed in the patents."). Lupin's Proposed ANDA Product ***lacks*** a label instructing use for the "treatment or prevention of the symptoms or effects of an HIV infection," thus precluding infringement.

#### 1. The plain and ordinary meaning of treating symptoms or effects of an HIV infection requires more than just treating an HIV infection.

The phrase "symptoms or effects of an HIV infection" was construed as having its "plain and ordinary meaning." (D.I. 126). ViiV never proffered a plain and ordinary meaning for "symptoms or effects of an HIV infection." Dr. Blick, without any further explanation, said the phrase "should include HIV infection." (Tr. 81:11-16). This makes no sense legally or logically; all Dr. Blick suggested with that testimony is the claims cover:

> **32**. A method for the treatment or prevention of ~~the symptoms or effects of~~ an HIV infection in an infected animal which comprises treating said animal with a therapeutically effective amount of a combination comprising (1S, 4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, and (2R, cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one.

Defining the symptoms or effects of an HIV infection to include treating the infection renders the "symptoms or effects" language a nullity.[8] Yet, when Dr. Blick was asked explicitly whether "a method for the treatment or prevention of an HIV infection falls within the scope of a method for the treatment or prevention of the symptoms or effects of an HIV infection," Dr. Blick demurred, saying "I don't know if I agree with you" because "these drugs treat, you know, the specific effect that is the replication of the virus." (Tr. 113:22-114:10). ViiV cannot meet its burden of proof when its own expert offers two mutually inconsistent opinions.

Dr. Blick's selective recitation of the patent specification is likewise unhelpful. Dr. Blick pointed to text stating one embodiment includes "the treatment and/or prophylaxis of HIV infections." (Tr. 83:5-10). Dr. Blick ignored the specification's ***alternative*** method embodiment (JX1 at col. 4, ln. 8 ("[t]he present invention also provides…")), one of which uses the "treatment or prevention of the symptoms or effects of an HIV infection" claim language. (*See id*. at col. 3, ll. 53-54). Nowhere in the specification do the inventors equate symptoms or effects of an HIV infection with the actual HIV infection itself.[9]

Dr. Blick also mischaracterized the articles he relied on as establishing an "ordinary

[8] Dr. Blick also based his opinion on his belief claims 20 and 32 do not "actually exclude HIV infections, so I think the treatment should be given its plain and ordinary meaning to include HIV infection." (Tr. 82:16-19). Dr. Blick's inclusion-by-exclusion approach is improper, notwithstanding his purported agreement "with the Court's construction opinion to give the phrase its plain and ordinary meaning," since all Dr. Blick can tell the Court is that the plain and ordinary meaning somehow includes treatment of an HIV infection. (Tr. 115:12-14).

[9] ViiV also had claims directed to the use of the combination for "treatment or prophylaxis of HIV infection" and a separate set directed to the "method for the treatment or prevention of the symptoms or effects," indicating the distinction between the two.

meaning" of "the symptoms or effects of an HIV infection." (Tr. 87:10-91:16). The articles Dr. Blick cited do not discuss the *symptoms or effects* of an HIV infection, only the three-drug combination's ability *to treat HIV infection itself*. (Tr. 90:7-8 (Fischl shows the three drug combination "has a definite treatment effect on HIV infection to reduce HIV viral load"); Tr. 90:22-24 (Van Dyke demonstrates "that the three-drug combination has anti-viral efficacy"); (Tr. 91:11-16 (Staszewski shows viral load reductions)). Dr. Langer[10] primarily relied on Dr. Blick for his opinion concerning the plain and ordinary meaning of the symptoms or effects of an HIV infection. (Tr. 196:21-197:1). Dr. Langer also admitted the three drug combination treats HIV infection, **not** its symptoms or effects. (Tr. 197:8-13 ("[W]hat the patent is telling you, and I'm just really reading it, is that you're effecting, at least from the specifications, the underlying disease, which is affecting the virus, *not some of the symptoms*, so to speak.") (emphasis added); *see also*, Tr. 197:21-22 ("[T]his would point to treating the underlying disease.")).

Dr. Blick also resorted to a "secondary effect" argument—that treating an HIV infection will eventually treat or prevent some symptoms or effects of the same HIV infection by "increas[ing] CD4 T helper cells" that typically battle infections in the body. (Tr. 83:18-23). This merely reflects a consequence of the drugs treating the HIV infection.[11] Even so, Dr. Blick did not go so far as to say alleviating all symptoms or effects of an HIV infection will necessarily occur via this secondary effect mechanism (Tr. 115:2-7), but opined that at best the combinations "secondarily *kind of help* opportunistic conditions." (Tr. 94:6-8 (emphasis added)).

Dr. Blick also failed to *quantify* how and when this "secondary effect" will occur, which

[10] Lupin maintains its objection to any of Dr. Langer's opinions concerning the treatment of HIV as he is not properly qualified as an expert in that area. (Tr. 181:19-182:8).

[11] Even Dr. Langer's effort to explain Dr. Blick's theory required him to admit all these drugs do is "treat[] the symptoms by inhibiting reverse transcriptase with *the result of suppressing HIV replication* that's happening no matter what." (Tr. 198:22-199:1 (emphasis added)).

is fatal to ViiV's attempt to infer a specific intent by Lupin to induce or contribute to infringement. *See Acorda Therapeutics, Inc. v. Apotex Inc.*, No. 07-4937, 2011 WL 4074116, at *19 (D.N.J. Sept. 6, 2011), *aff'd*, 476 Fed. App'x 746 (Fed. Cir. 2012) (even assuming direct infringers, "the Court is unwilling to infer intent based upon information that must be pieced together in a puzzle" and "particularly where the potentially infringing use is such a small subsection of the market"); *Toshiba Corp. v. Imation Corp*., 681 F.3d 1358, 1362 (Fed. Cir. 2012) (for contributory infringement, "the patent owner must show, among other things, that there are no substantial non-infringing uses" including the frequency of uses).

Nor has ViiV presented a viable doctrine of equivalents theory. Dr. Blick did not testify on the theory; Dr. Langer is not qualified[12] to offer his conclusory[13] medical equivalence opinions. (D.I. 203, Pl. Br. at 17). Even so, equating treating an HIV infection to treating symptoms or effects of the infection (a) vitiates the "symptoms or effects" claim element; and (b) fails under the disclosure-dedication rule discussed in Section B(2)(c), above, since the specification specifically discusses the treatment of HIV infection. (JX 1 at col. 3, ll. 34-36).

**2. Lupin's proposed ANDA labeling does not identify any symptoms or effects of an HIV infection that its product is indicated to treat.**

Lupin's proposed label states that Lupin's proposed ANDA product is only "indicated in combination with other antiretrovirals or alone for the treatment of HIV-1 infection." (PTX152 at 12340; Tr. 92:14-23, 93:7-19 ("the Medication Guide refers to the three-drug combination

[12] Dr. Langer lacks knowledge about the treatment of HIV. Dr. Langer admitted that he is not a medical doctor, has never prescribed *any* drug, nor does he know how retail pharmacists will rely on a drug's label. (Tr. 204:1-16). As such, Dr. Langer is not competent to provide medical expert testimony on the treatment of HIV, much less any potential inducement on Lupin's part.

[13] The "doctrine of equivalents is not a talisman" designed as a catch-all in case a literal infringement theory fails; rather, "it is a limited remedy available in special circumstances, the evidence for which is the responsibility of the proponent." *Schoell v. Regal Marine Indus., Inc.*, 247 F.3d 1202, 1210 (Fed. Cir. 2001); *Zelinski*, 185 F.3d at 1317 (affirming the district court's grant of Brunswick's motion for summary judgment of noninfringement under the doctrine of equivalents because the only evidence submitted by patentee was a conclusory statement).

being used to treat HIV infection.")). Dr. Blick admitted that Lupin's proposed label nowhere discusses "symptoms or effects" of an HIV infection. (Tr. 112:14-19). Dr. Blick did acknowledge there were several diseases, many of which are listed in the '191 patent specification (JX1 at 3:41-50), perceived as "symptoms or effects" of an HIV infection, such as pneumonia, Kaposi's sarcoma, thrombocytopenic purpura and others (Tr. 116:19-118:15). None of these appear in Lupin's proposed label indications either. (Tr. 119:14-120:13; PTX152).

Thus, contrary to ViiV's theory, Lupin's label *does not* instruct users to perform the infringing method, precluding an indirect infringement finding. *See AstraZeneca Pharms. L.P. v. Apotex Corp.*, 669 F.3d 1370, 1380 (Fed. Cir. 2012); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010) (indirect infringement requires proof the proposed labeling instructs users to perform the patented method and teach an infringing use such that the court is willing to infer from those instructions an affirmative intent to infringe the patent).

**3. There is no indirect infringement of the asserted method claims.**

There is no indirect infringement absent an act of direct infringement. *See Convolve, Inc. v. Compaq Computer Corp.*, __ Fed. App'x __, No. 2012-1074, 2013 WL 3285331, at *17 (Fed. Cir. July 1, 2013) (citing *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1317 (Fed. Cir. 2009)). As discussed in Section II(B) above, there is no evidence of direct infringement even if patients use Lupin's ANDA product due to the use of abacavir sulfate salt instead of free base.

Proof of indirect infringement requires ViiV to additionally show Lupin "possessed a *specific intent* to encourage another's infringement of the patent." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1328 (Fed. Cir. 2009) (emphasis added); *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1304 (Fed. Cir. 2006) (en banc in relevant part). ViiV hasn't met its burden of proof on that prong of the test either.

**a. No evidence of § 271(b) inducement.**

As noted in Section II(C)(2), ViiV had the burden to show not only that Lupin's label instructions instruct doctors or patients to use the claimed method, but also that the instructions are sufficient to infer a specific intent to encourage infringement by Lupin. *See Aventis Pharma Deutschland GmbH v. Cobalt Pharms., Inc.*, 355 F. Supp. 2d 586, 599 (D. Mass. 2005) (no intent inference when doctors would not read label as suggesting using the drug in patented method). ViiV introduced no such evidence of intent by Lupin witnesses; made no effort to quantify the number of directly infringing patients; and Dr. Blick admitted that doctors in this field get information on using drugs not from generic companies, but a plethora of sources. (Tr. 120:23-123:5). Lupin's proposed label instructs people how to treat an HIV infection, not the symptoms or effects of an HIV infection. (*See* PTX 152; Tr. 92; 15-23; 93:7-12, 197; 202:10-13).

ViiV also relies on Dr. Langer's testimony. (D.I. 203, Pl. Br. at 19-20). Dr. Langer refers to "a letter to ViiV" as evidence of Lupin's intent. (Tr. 202:10-11). He cites to PTX 152, the Lupin label, which as noted above does not evidence intent to indirectly infringe.

ViiV must also show that Lupin did not have a reasonable belief that the Asserted '191 patent claims are invalid. *Commil USA, LLC v. Cisco Sys., Inc.*, ___ F.3d ___, No. 2012-1042, 2013 WL 3185535, at *6 (Fed. Cir. June 25, 2013) ("a good-faith belief of invalidity may negate the requisite intent for induced infringement"). ViiV utterly lacks evidence on this point.

**b. No evidence of contributory infringement.**

Contributory infringement requires showing the alleged infringer "knew that the combination for which his component was especially designed was both patented and infringing." *Aro Mfg. Co. v. Convertible Top Replacement Co.*, 377 U.S. 476, 488 (1964). "Unless a commodity 'has no use except through practice of the patented method,' the patentee has no right to claim that its distribution constitutes contributory infringement." *Sony Corp. of*

*Am. v. Universal City Studios, Inc.*, 464 U.S. 417, 441 (1984) (quoting *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 198 (1980)).

ViiV relies on Dr. Langer's testimony that "the only use that I've heard of for this product is the treatment of HIV infection." (Tr. 203:3-6). That confirms Lupin will *not* contribute to the infringement of the '191 patent, which requires "treating symptoms or effects of an HIV infection"; and that the product has substantial non-infringing uses. (*See* PTX152; Tr. 92:15-23; 93:7-12, 202:10-13). ViiV's "secondary effects" theory does not work since ViiV never quantified the number of patients who will or will not experience such secondary effects. *See* Section II(C)(1), above. ViiV thus has not met its burden on contributory infringement.

**D. ViiV has not shown it is entitled to any remedy.**

To claim a remedy, ViiV must show the "infringing feature drives consumer demand for the accused product." *Apple Inc. v. Samsung Elecs. Co.*, 695 F.3d 1370, 1375 (Fed. Cir. 2012). ViiV presented no such evidence; its fact and expert witnesses admitted any loss of revenue and market share would result from Lupin's lower product price. (Tr. 860:22-861:14, 1167:19-23). The district court also retains discretion to enter an injunction even in ANDA cases. *See SmithKline Beecham Corp. v. Apotex Corp.*, 247 F. Supp. 2d 1011, 1045-52 (N.D. Ill., 2003), *vacated on other grounds*, 403 F.3d 1331 (Fed. Cir. 2005). To obtain an injunction, ViiV must show irreparable injury; that the remedies available at law are inadequate; that considering the balance of hardships, an equitable remedy is warranted; and that the public interest would not be disserved by a permanent injunction. *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 391 (2006); *Ecolab, Inc. v. FMC Corp.*, 569 F.3d 1335, 1351-52 (Fed. Cir. 2009). ViiV UK, purported patent owner, experiences no irreparable harm—it does not itself sell product. If Lupin enters the market, only non-party GSK may lose sales (*see* Tr. 856:6-858:5), but that is "monetary harm," which is not irreparable harm, even if it could be imputed to ViiV. ViiV made

no attempt to show irreparable harm. If Lupin enters the market, ViiV can compete on price; if ViiV refuses and loses revenue, ViiV has "monetary harm" which "is not irreparable harm." *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1338 (Fed. Cir. 2012).

A permanent injunction is not in the public interest. Hatch-Waxman is designed to "speed[] the introduction of low-cost generic drugs to the market." *Federal Trade Comm'n v. Actavis, Inc.*, 133 S. Ct. 2223, 2228 (2013). Public policy favors "eliminating unwarranted patent grants so the public will not 'continually be required to pay tribute to would-be monopolists without need or justification.'" *Id.* at 2233. ViiV's website admits high drug cost can deter patients from receiving care. (Tr. 866:5-8). Since lack of access to these drugs can be a death sentence (Tr. 311:17-24, 865:8-867:6), an injunction is not in the public interest either.

***LPI.*** ViiV's brief failed to articulate the basis for its claim against LPI save to assert LPI "will be involved in marketing and distribution of the generic product in the United States." (D.I. 203, Pl. Br. at 6-7). That is insufficient under ViiV's cited cases, the only one of which outside a motion to dismiss relied upon a degree of corporate intertwinement and involvement in the application that ViiV failed to comparably prove at trial. Thus, *Smithkline Beecham Corp. v. Geneva Pharms., Inc.*, 287 F. Supp. 2d 576, 584-585 (E.D. Pa. 2002) ("[b]y its terms, the Act limits liability for direct infringement to the party submitting the ANDA" and rejecting the premise that "that "a third party can be liable as a direct infringer under Section 271(e)(2) based on its 'participation' in another party's filing of an ANDA") and *Smithkline Beecham Corp. v. Pentech Pharms., Inc.*, No. 00 C 2855, 2001 WL 184804, at *3 (N.D. Ill. Feb. 20, 2001) apply.

## CONCLUSION

ViiV failed to prove that Lupin will infringe the Asserted Claims either literally or under the doctrine of equivalents, or that it is entitled to the remedy requested. Lupin respectfully requests that the Court enter judgment in favor of Lupin on these issues.

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